REMARKS

1. Rejection of Claims 21-24 and 27-31 under 35 U.S.C. 112, first paragraph

Claims 21-24 and 27-31 were rejected under 35 U.S.C. 112, first paragraph, written description, for the reasons of record.

Initially, Applicants note that independent Claims 21 and 27 have been amended to recite an isolated protein having SEQ ID NO:4, and variants thereof that are at least 95% identical to SEQ ID NO:4 and have cuticlin activity. Support may be found on page 26, line 18 through page 27, line 2 which contemplates protein variants, and on page 64, lines 12-16 which describes an activity of recombinantly expressed cuticlin proteins of the present invention.

In so amending, Applicants have attempted to follow the guidance set forth in Training Example No. 14 of the Synopsis of Application of Written Description Guidelines, which was prepared by the USPTO to train Examiners how to apply the requirements set out in Federal Register, Vol. 66, No. 4, pages 1099-1111.

Training Example 14 describes a hypothetical specification which discloses a single protein species, SEQ ID NO:3, which catalyzes the reaction of A to B. The specification contemplates, but does not exemplify, variants having the same activity. The specification further indicates that procedures for making variants are routine and provides an assay for testing such variants for activity. Based upon the foregoing, the applicant in Example 14 claims a protein having SEQ ID NO:3 and variants that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A to B.

The USPTO analyzed the adequacy of the written description of Example 14 as follows. "The single species disclosed is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO:3 which are capable of the specified activity. One of skill in the art would conclude that applicant was in **possession of the necessary common attributes** possessed by the members of the genus" (emphasis added). Applicants note that the USPTO analysis correctly concludes that description of the necessary common attributes of the genus is what is required to satisfy 35 U.S.C. 112, first paragraph, and not physical possession of some arbitrary number of species exhibiting that activity. Accordingly, Applicants respectfully assert, and argue that the USPTO analysis concurs, that a single disclosed species can adequately define a genus of structurally similar molecules having the same functional property, and is thus consistent with the requirements as set forth in *Regents of the University of California v. Eli Lilly and Company*, 119 F3d at 1569, 43 USPQ2d at 1406, which calls for "recitation of a representative number of polypeptide sequences *** **or of a recitation of structural features common to the genus**" (emphasis added).

In view of the foregoing, Applicants respectfully request withdrawal of the Examiner's rejection of 21-24 and 27-31 under 35 U.S.C. 112, first paragraph.

2. Rejection of Claims 21-24 and 27-31 under 35 U.S.C. 112, first paragraph

Claims 21-24 and 27-31 were rejected under 35 U.S.C. 112, first paragraph, enablement, for the reasons of record. Generally, the Examiner's rejection appears to focus on the issue of

protein variants and whether or not sufficient guidance is provided to teach one of skill in the art which residues may be modified and still retain protein function.

Applicants respectfully argue that the Examiner's position is not supported by case law. The case most often cited when addressing the issue of predictability is *In re Fisher*, 166 USPQ 18 (CCPA 1970), which is typically cited for the general proposition that the more unpredictable an area is, the more specific enablement is necessary. However, *In re Fisher* does not support the Examiner's position that predicting functionality is required to satisfy the first paragraph of 35 USC 112. To address that issue, cases decided after *In re Fisher*, which provide additional guidance and refinement, must be considered by the Examiner.

The Examiner's position in the instant application is similar to that set forth by the dissenting opinion of *In re Angstadt*, 537 F.2d 498, 190 USPQ 214 (CCPA 1976). In that case the inventors appealed a board decision holding undue experimentation would be required to determine which of thousands of possible combinations would work to produce hydroperoxides in their claimed catalytic process. As in *In re Fisher*, the court determined that the claimed process was an "unpredictable" art. The dissent argued that the disclosure must provide "guidance which will enable one skilled in the art to determine, *with reasonable certainty before performing the reaction*, whether the claimed product will be obtained" (emphasis in original) *In re Angstadt*, 190 USPQ at 222. The majority rejected this approach, arguing that under the dissent's standard, "all 'experimentation' is 'undue' since the term 'experimentation' implies that the success of the particular activity is *uncertain*. Such a proposition is contrary to the basic policy of the Patent Act", *In re Angstadt*, 190 USPQ at 219. The majority continued, "What the

dissent seems to be obsessed with is the thought of catalysts which *won't* work to produce the intended result. Without undue experimentation or effort or expense the combinations which do not work will readily be discovered and, of course, nobody will use them and the claims do not cover them." (emphasis in original), *In re Angstadt*, 190 USPQ at 219.

Applying the reasoning of the majority of *In re Angstadt* to the present application, Applicants respectfully argue that 35 U.S.C. 112 does not require the specification to set forth teachings in order to predict changes that can be made and still retain a protein with cuticlin activity. Rather, what is required is that one of skill in the art must have sufficient guidance to be able to determine whether or not a given protein falls within the scope of the claim. Applicants argue that this can be readily accomplished by comparing the protein sequences and determining if the protein in question has the activity described in the specification. See *In re Wands* 8 USPQ2d 1400, 1404 in which the court held routine screening does not constitute undue experimentation. Similar to the process of *In re Angstadt*, Applicants acknowledge that sequences may exist which are 95% or more identical and which do not cuticlin activity, but as set forth by the court, such sequences should not be used as the focal point in analyzing the question of undue experimentation, and in any case are not covered by the claims.

The Court of Appeals for the Federal Circuit (CAFC) has upheld the holding of *In re Angstadt* on many occasions, including in biotechnology cases. For example, in *Amgen Inc. v. Chugai Pharmaceutical Co.*, 18 USPQ 1016, 1027 (CAFC 1991) the court cited *In re Angstadt* as standing for the proposition that "it is not necessary that a patent applicant test all the embodiments of his invention". In applying *In re Angstadt* to a biotechnology case, the *Amgen*

court argued that while an applicant need not test all embodiments, the law still requires the applicant to "provide a disclosure sufficient to enable one skilled in the art to carry out the invention commensurate with the scope of his claims. For DNA sequences, that means disclosing how to make and use enough sequences to justify grant of the claims sought. Amgen has not done that here." *Amgen Inc. v. Chugai Pharmaceutical Co.*, 18 USPQ at 1027.

In applying *Amgen* to the instant application, Applicants argue that one must resist the temptation to focus on the court's use of the term "enough sequences" without first reviewing the claims sought by Amgen. In fact, Amgen was seeking claims not limited to any particular sequence or defined activity, i.e. Amgen's claims were to any DNA sequence encoding a protein "whose activity has not been clearly ascertained" *Amgen Inc. v. Chugai Pharmaceutical Co.*, 18 USPQ at 1028. Therefore, although the application did contain nucleic acid sequence information, the sequences did not appear in the claims and there was insufficient guidance with respect to determining which proteins contained EPO activity. Accordingly, one of skill in the art was not provided either structural or functional guidelines for determining whether or not a given protein fell within the scope of the claims.

The claims in the instant application are narrow compared to those sought by Amgen and the instant specification provides one of skill in the art defined nucleic acid and amino acid sequences, methods for determining whether a given sequence is 95% identical to the specified sequence and a method for determining whether a given protein has cuticlin activity. Accordingly, unlike in *Amgen*, one of skill in the art is provided both structural and functional guidelines for determining whether or not a given protein falls within the scope of the claims and

therefore the instant specification satisfies 35 U.S.C. 112, 1st paragraph as set forth in *In re Angstadt.*

In view of the foregoing, Applicants respectfully request withdrawal of the Examiner's rejection of 21-24 and 27-31 under 35 U.S.C. 112, first paragraph.

In the event the Examiner has any questions regarding this application, the Examiner is invited to contact the undersigned attorney at (970)493-7272.

Respectfully submitted,

Dated: August 26, 2003

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